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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/300,482	CHEIKH ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,10-13,15-22 and 24-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,10-13,15-22 and 24-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. All rejections and rejections not repeated below are hereby withdrawn. Claims 1-2, 10-13, 15-22, and 24-31 are pending.

Claim Rejections - 35 USC § 101

Claims 1-2, 10-13, 15-22, and 24-31 are again rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

The arguments filed 2/2/04 have been fully considered but are not persuasive. In response to the argument that the claimed nucleic acids may be used to identify polymorphisms in plants, it is again noted that none of the claimed sequences are disclosed as having a polymorphic site, or as being known to be associated with a polymorphism. In the absence of such a disclosure or knowledge present in the prior art, further research is required to determine if any of the claimed sequences comprises or is associated with a polymorphism or polymorphic site. Applicant is reminded that a "use" to do further research is not a specific, substantial and credible utility under 35 USC 101. See MPEP 2107.

In response to the argument that the asserted utilities are "legally insufficient simply because other molecules can be used for the same purpose", it is noted that the examiner actually stated that the uses disclosed are *generic* to the *class* of nucleic acids, and therefore do not represent substantial, specific, and credible utilities for the specific nucleic acid sequences claimed. For example, ANY nucleic acid molecule may be used in hybridization assays (to identify homologs, in microarrays, etc.); the "utility" of the result depends on the particular nucleic acids used. What is the "immediate use" to a scientist of a homolog to a nucleic acid which itself has no known activity, and/or is not known to encode a protein with a known

activity? It may be scientifically interesting to discover that several organisms comprise sequences with some degree of similarity, but further research is still necessary to discover what the sequences DO or may be used for.

In response to the argument comparing the instant sequences to a golf club, it is noted that golf clubs are a completely different statutory category from nucleic acids. In addition, a golfer (one skilled in the art) would immediately know the "use" of a golf club (i.e. a golf club has a well-known utility which is specific, substantial and credible). However, one skilled in the art of golf would not accept that all STICKS (the generic "class") had a specific, substantial and credible utility based on the well-known use of golf clubs; according to this analogy, one would impute a "golf club" utility to baseball bats and hockey sticks!

In the instant case, applicants have repeatedly argued that the claimed sequences encode phosphogluconate pathway enzymes. As previously set forth and maintained in previous office actions, the specification does not actually disclose that any of the claimed SEQ ID NO's is known to encode a protein or peptide, specifically one of the enzymes recited in the claims. For the nucleic acid to have utility based on a putatively encoded peptide, the identity and activity of the peptide must be known or established. In response to the argument that the claims also recite "fragments", thus the a complete ORF is not necessary, it is again noted that a fragment of a protein, wherein the fragment itself does not have utility or activity, does not necessarily have a utility.

In the instant case, it is again noted that each nucleic acid molecule claimed has at least one (in most cases, several) ATG "codons". However, as it is not known for ANY of the claimed sequences what the ORF is, it is unknown whether any sequence is actually translated into a peptide, or, if translated, what the activity or function of that peptide may be. For example, SEQ ID NO: 14 comprises six "ATG" codons, but it is not known which, if any, is the start codon for a

6-phosphogluconate dehydrogenase. As set forth in the office action of 12/20/00, none of the claimed SEQ ID NO's appears to be long enough to encode the entirety of the enzyme disclosed by the specification to be putatively encoded thereby. It is possible that a claimed SEQ ID NO: encodes a fragment of an enzyme; however, it is not disclosed whether that fragment has activity or another function such that the fragment has utility under 35 USC 101. In response to the argument that fragments may be used as probes, it is noted that a "probe" (i.e. for a homologous sequence) for a sequence of unknown function does not impute utility to the probe itself. There is no evidence in the instant specification, and none has been filed to show or support that any of the claimed nucleic acids do, in fact, encode ANY peptide, specifically one with enzymatic activity.

As the instant specification does not disclose, and the prior art does not teach, that the instantly claimed nucleic acid sequences actually encode any protein or peptide, specifically the enzymes recited in the claims, the nucleic acid sequences represented by SEQ ID NO's 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619 do not have utility based on utility of a protein encoded thereby. For all the reasons previously set forth and set forth above, the rejection is maintained.

Claims 1-2, 10-13, 15-22, and 24-31 are also rejected under 35 U.S.C. ' 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention. As the utility rejection is maintained, so is the enablement rejection.

Claim Rejections - 35 USC § 112

Claims 1-2, 22, and 24-25 are again rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an ENABLEMENT rejection.

Applicant's arguments filed 2/2/04 have been fully considered, but are not persuasive. In response to the argument that the claims are not directed to enzymes, it is noted that the claims ARE directed to nucleic acids limited to encode particular enzymes. As one skilled in the art would not know how to use the inventive nucleic acid sequences to make the particular enzymes recited in the claims for the reasons previously set forth, the claims are not enabled. In response to the argument that sequence alignment, molecular weight determination and antibody assays are routine and do not constitute undue experimentation, it is noted that none of these assays would positively confirm that a nucleic acid sequence does, in fact, encode a peptide with a particular enzymatic activity. For example, claim 1 recites nucleic acids encoding a particular dehydrogenase, a particular epimerase, and a particular isomerase. As previously set forth, one skilled in the art would first have to determine IF a nucleic acid sequence actually comprises an ORF or ORF's, and if multiple ORF's are present, which one to use in continuing steps. The peptide encoded by the chosen ORF would have to be synthesized, then tested in an assay to determine if the chosen peptide(s) do, in fact comprise the activity claimed for the particular substrate. It is admitted that identification of ORFs and peptide synthesis are fairly routine. However, not all synthetic proteins, even of a correct sequence, will have a desired activity due to possible tertiary and quaternary structure considerations. The art of enzymatic synthesis is very complex and requires as much luck as skill in some instances to synthesize an

active enzyme. One may instead express a protein by cloning a nucleic acid sequence into a vector, then into a cellular expression system. In this case, one must determine an appropriate vector, must choose regulatory sequences, etc. which allow for proper translation of the protein, must choose an appropriate cell system, and must determine purification conditions such that any enzymatic activity is not lost (e.g. due to denaturation, N-terminal blockage, inclusion bodies, etc.) One a protein is synthesized or expressed, and purified, one skilled in the art must know how to test that the protein does indeed have the required enzymatic activity and is specific for the substrates recited in the claims. The examiner maintains that, due to uncertainty in the art for how to synthesize or express any active enzyme from a nucleic acid not known to actually encode that enzyme, and the lack of teaching in the specification for how to test for the particular activities claimed once any peptide putatively encoded IS synthesized, the specification does not provide an enabling disclosure for claims directed to nucleic acids encoding recited enzymes.

For these reasons and those previously set forth, the rejection is maintained.

35 U.S.C. 112, Written Description Rejection

Claims 1-2, 10-13, 15-22, and 24-30 are again rejected, as previously set forth in multiple office actions, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed 2/204 have been fully considered but they are not persuasive. Applicant's arguments are addressed below.

The specification discloses SEQ ID NO's 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619. which putatively encode various phosphogluconate pathway enzymes. Sequences consisting of SEQ ID NO's 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619 meet the written description provisions of 35 USC 112, first paragraph. However, claims 1, 2, 10-22, 24-30 recite open claim language (comprising) and claims 1, 10, 24, and 26 are specifically directed to encompass sequences that hybridize to the claimed SEQ ID NO's. As the sequences recited in the claims are apparently fragments which do not appear to comprise ORF's or actually encode any known proteins, a nucleic acid "comprising" the fragments encompasses much larger sequences which may encode entirely different proteins from those recited, encompasses genomic sequences which may also comprise introns, noncoding regions, etc. In particular, a genomic sequence significantly longer in length than a claimed fragment may still hybridize to a recited sequence under the claimed conditions as introns, etc. may "bubble" out where mismatches occur but still allow for sufficient length of the genomic sequence to anneal under the claimed conditions. The specification sets forth a list of possible variations for the inventive sequences, as argued by applicant, but does not actually describe, by sequence or structure, any of the variations, nor does the specification disclose any longer sequences (e.g. genomic) which may comprise the claimed sequences. For these reasons, the examiner maintains that the specification provides insufficient written description to support the genus encompassed by the claim.

Applicant argues that he need describe only the claimed invention, and insists that he has done so. In response, it is noted that the specification does not actually describe any nucleic acid KNOWN to encode an entire enzyme, as recited in claims 1-2, 22, 24, and 25. The specification does not disclose or describe an ORF for any nucleic acid, and therefore does not describe the claimed invention of at least claims 1-2, 22, 24, and 25.

Applicant argues that the specification describes gene sequences, corresponding sequences from other species, mutated sequences, SNPs, polymorphic sequences, promoter sequences, exogenous sequences, and so forth. In fact, the specification discloses that the inventive sequences *may encompass* gene sequences, corresponding sequences from other species, mutated sequences, SNPs, polymorphic sequences, promoter sequences, exogenous sequences, but does not actually describe, by sequence or structure, the sequences represented by gene sequences, corresponding sequences from other species, mutated sequences, SNPs, polymorphic sequences, promoter sequences, exogenous sequences, etc. anywhere. As previously set forth and reiterated above, gene sequences may comprise a variety of ORFs, exons, noncoding regions, repetitive sequences, etc., none of which are described by the instant specification. The specification does not describe or exemplify mutated sequences, SNPs, or polymorphic sequences comprising or comprised within the claimed SEQ ID NO's anywhere. It is generally accepted in the art that mutations and polymorphisms are somewhat unpredictable, both in sequence and frequency, therefore mere disclosure that a sequence MAY be mutated or comprise a polymorphism is not a description of the large variety of sequences embodied.

With regard to claims reciting hybridization language, it is not true, as argued by applicant, that every member of the genus embodied by the claims comprises a common structural feature; i.e. one of the claimed SEQ ID NO's. A long sequence with complementary regions interspersed by non-complementary regions (e.g. a gene comprising introns) may hybridize to a claimed sequence wherein the non-complementary regions "bubble out", but sufficient length of the sequence complements a claimed SEQ ID NO: to meet the claimed hydridization conditions. Due to the interspersed non-complementary regions, the long

sequence (gene) will NOT comprise the SEQ ID NO: to which it hybridizes. The specification fails to describe any sequence which does not *consist of* a claimed SEQ ID NO.

As previously set forth in various office actions, the examiner has closely examined the specification for any kind of support or evidence that the claimed nucleic acids actually do encode the recited proteins. Applicant has provided no evidence beyond that of the specification to show that the claimed nucleic acids encode the particular enzymes recited in the claims. Table A of the specification discloses sequence similarity information (e.g. % identity) between peptides putatively encoded by the claimed sequences and sequences which encode known enzymes, but does not disclose any comparison of binding regions, conserved regions, catalytic regions, etc. to support that the peptides putatively encoded by the claimed SEQ ID NO's would be expected to actually exhibit ANY enzyme activity. As previously set forth, BAKER teaches that structural (de novo) models are more accurate at predicting functional homologies between proteins, especially where sequence comparison fails (p. 94). Applicant argues that a detailed chemical structure; i.e. the claimed nucleic acid sequences are disclosed in the instant specification. While the nucleic acid sequences represented by the claimed SEQ ID NO's are fully described by the specification at the time of filing, nucleic acid sequences *encoding the proteins* recited in the claims were not fully described as set forth above. The specification does not disclose that the claimed nucleic acid sequences actually encode any proteins or peptides, as previously set forth and reiterated above, therefore nucleic acid sequences encoding the claimed proteins AND comprising the claimed SEQ ID NO's were not described in the specification as originally filed.

It is noted that while a nucleic acid sequence is a chemical structure, a nucleic acid "structure" is not the same as a peptide or protein structure, and is not necessarily predictive of a protein structure putatively encoded thereby. Given the acknowledged controversy in the art

over whether sequence similarity alone can be used to accurately predict function, and the lack of teaching in the specification for whether any of the claimed nucleic acids actually encodes any protein, specifically one of the recited enzymes, and absent factual evidence to the contrary, one skilled in the art would reasonably doubt that sequence similarity alone is sufficient to predict whether the biological and enzymatic activity of the claimed subject matter is the same as that of the prior art. The specification fails to describe ANY nucleic acid actually encoding one or more of the claimed enzymes, therefore the rejection is maintained.

With the exception of sequences consisting of SEQ ID NO's 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. For all of the reasons set forth above and previously set forth, the rejection is maintained.

Claims 1, 22, 24, and 25 recite a "substantially purified nucleic acid" which encodes a "maize or soybean phosphogluconate pathway enzyme" wherein the nucleic acid is a specific SEQ ID NO: or hybridizes to specific SEQ ID NO's. The specification fails to describe any "substantially purified nucleic acid sequence" which is known to encode a maize or soybean phosphogluconate pathway enzyme. Once purified, nucleic acid and peptide sequences do not carry information with regard to their origin. An enzyme expressed from a nucleic acid will display activity, under appropriate conditions, no matter what system, cell line, clone, etc. it is expressed from/in. A purified sequence (comprising a complete ORF) may be cloned into another plant/cell line and a protein expressed; is the protein still a "maize or soybean" enzyme? In addition, it is noted that sequences which hybridize to one of the claimed nucleic

acids under the conditions recited, and encode one of the recited enzymes, but are NOT sequences purified from maize or soybean are known in the art (see e.g. the sequence taught by MARTIN et al., set forth in the previous office action). Applicant has not set forth any arguments specific to this rejection and the examiner maintains that the specification fails to describe a "substantially purified nucleic acid" which encodes a "maize or soybean" enzyme, therefore the rejection of claims 1, 22, and 24-25 is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon. to Wed, 7:30-4; Thurs 7:30-6; Fri 7-1 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
4/5/04

mam